REMARKS

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

Rejoinder of Claims

Applicants continue to request the rejoinder of claims 13-15, 20, 21 and 49 directed to methods of using the claimed polynucleotides upon allowance of a product claim per the Commissioner's Notice in the Official Gazette of March 26, 1996, entitled "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103 (b)" which sets forth the rules, upon allowance of product claims, for the rejoinder of process claims covering the same scope of products. Therefore, since it appears a product claim will be allowed, Applicants respectfully request rejoinder and examination of method claims 13-15, 20, 21 and 49.

Amendments to the Claims

Claims1 b) and claim 11 have been amended in the interest of expediting prosecution, i.e., to obviate the § 112, first paragraph (written description) rejection, and not for reasons related to patentability. Claim 1 b) has also been amended to include the functional activity of "cyclic nucleotide phophodiesterase activity" with respect to polypeptides at least 90% identical to the amino acid sequence of SEQ ID NO:1. Claim 11 has also been amended to include "encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:1 and said polypeptide having cyclic nucleotide phosphodiesterase activity." Support for each amendment can be found throughout the specification, for example at page 15, lines 9-15 and page 16, lines 3-13 and lines 26-29.

Claim 8 has been amended to correct a typographical error and claims 4, 9, 12 and 23 have been deleted in the interest of expediting prosecution and not for reasons related to patentability. Entry of these amendments is respectfully requested.

Rejection under 35 U.S.C. §112, first paragraph

Claims 3, 6-8 and 11 stand rejected under the first paragraph of 35 U.S.C. §112 for allegedly containing subject matter "not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." It is asserted at page 3 of the August 29, 2002 Office Action that there is insufficient written description of a polypeptide having 90-99% sequence identity to SEQ ID NO:1 or a polynucleotide of 90-99% sequence identity to SEQ ID NO:2 which would still maintain the function of the polypeptide.

A. Legal Requirements

> . . . the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed. Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991)

Attention is also drawn to the Patent and Trademark Office's own "Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1", published January 5, 2001, which provide that:

> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics[42] which provide evidence that applicant was in possession of the claimed invention,[43] i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.[44] What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail.[45] If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met.[46]

Thus, the written description standard is fulfilled by both what is specifically disclosed and what is conventional or well known to one skilled in the art.

B. The Specificati n provides an adequate written description of the claimed "variants" of SEQ ID NO:1 and SEQ ID NO:2.

The subject matter recited in amended claims 3 and 11 is adequately disclosed in the Specification given what is are conventional or well known to one skilled in the art.

Please note that the "variant" language of independent claim 3 has been amended to claim "a polypeptide comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1, said polypeptide having cyclic nucleotide phosphodiesterase activity." It is submitted that the Specification provides an adequate written description of the claimed variants of SEQ ID NO:1 to convey with reasonable clarity to those skilled in the art that applicants were in possession of the invention as "now" claimed at the time of the filing of this application.

Variants of SEQ ID NO:1 are defined in the Specification at, for example, page 4, lines 7-9; page 14, line 28 to page 15, line 6; and page 16, lines 26-29. Polypeptide sequence variants are know by one of skill in the art to have amino acid substitutions which do not alter the function of the polypeptide. For example, a change of an amino acid residue to another at the extreme amino- or the caroboxy-terminus of the sequence most likely will not alter the function of the polypeptide. The Specification defines specific structural domains related to PDE proteins at page 15, linc 17 to page 16, line 2. Structural domains within PDE9A are two potential divalent cation binding sites that function within the catalytic region of PDEs to regulate the intracellular concentrations of cyclic nucleotides and their effects on signal transduction. This catalytic region with its two divalent cation binding sites is conserved in all three PDE proteins presented in Figure 2 and PDE9A also shares similar homology in the catalytic domain to other members of PDE families 1, 2, 3, 4, 5, 6, and 7 (see Specification, p. 15, line 30 to p. 16, line 2). Accordingly, it is well within the skill of those in this art to identity those polypeptides comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1 and that these polypeptide variants retain the cyclic nucleotide phosphodiesterase activity.

Furthermore, an assay to measure cyclic nucleotide phosphodiesterase activity is defined in the specification at page 52, Example X. Assays to determine functional activity are considered routine experimentation when identifying functional sequence variants. One of ordinary skill in the art would recognize polypeptide sequences which are variants having at least

90-99% amino acid identity to SEQ ID NO:1, as those polypeptide sequences which, when assayed, have cyclic nucleotide phosphodiesterase activity. Accordingly, polypeptides comprising an amino acid sequence that is 90-99% identical to the amino acid sequence of SEQ ID NO:1 can easily be identified by one of skill in the art based on both the presence of functional and structural domains and by the assay all disclosed in the Specification. Accordingly, Applicants have disclosed the claimed invention in sufficient detail and provided identifying characteristics such that the skilled artisan would understand that Applicants were in possession of the claimed invention. Therefore, the specification provides an adequate written description of the claimed variants of SEQ ID NO:1 to convey with reasonable clarity to those skilled in the art that applicants were in possession of the invention as "now" claimed at the time of the filing of this application.

Please note that the "variant" language of independent claim 11 has been amended to claim "a polynucleotide comprising a polynucleotide sequence at least 90% identical to the polynucleotide sequence of SEQ ID NO:2, encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:1 and said polypeptide having cyclic nucleotide phosphodiesterase activity." It is submitted that the Specification provides an adequate written description of the claimed variants of SEQ ID NO:2 to convey with reasonable clarity to those skilled in the art that Applicants were in possession of the invention as "now" claimed at the time of the filing of this application.

Variants of SEQ ID NO:2 are defined in the Specification at, for example, at page 17, lines 3-9. The present application is directed, *inter alia*, to polynucleotides encoding PDE proteins, including polynucleotides encoding PDE9A related to the amino acid sequence of SEQ ID NO:1. The skilled artisan is aware that due to the degeneracy of the genetic code, there are alternative codons which when present in sequence variants of the polynucleotide sequence of SEQ ID NO:2 would still encode a polypeptide comprising the amino acid sequences of SEQ ID NO:1 and the polypeptide would have the cyclic nucleotide phosphodiesterase activity. For example, the amino acid" histidine" is encoded by either the codon "CAU" or "CAC", a change at the third position of the codon, either "U" or "C" does not alter the amino acid for which it encodes. Likewise, the amino acid "leucine"can be encoded by "UUA," "UUG," "CUU,"

"CUC," "CUA," and "CUG," where only the second position of the codon is invariant. Thus, one skilled in the art is well versed in the degeneracy of the genetic code.

Claim 11 b) is further defined in that the claimed polynucleotide sequence encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:1 and this polypeptide has to retain the cyclic nucleotide phosphodiesterase activity. As a result, it is well within the skill of those in the art to identify those polynucleotides comprising a polynucleotide sequence at least 90% identical to the polynucleotide sequence of SEQ ID NO:2 which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:1 and this polypeptide has cyclic nucleotide phosphodiesterase activity for the reasons submitted above with regards to the claimed polypeptide variants. Accordingly, Applicants have disclosed the claimed invention of claim 11 in sufficient detail and provided identifying characteristics of the amino acid sequence of SEQ ID NO:1 encoded by the polynucleotide of SEQ ID NO:2 and variants thereof, such that the skilled artisan would understand that Applicants were in possession of the claimed invention. Therefore, the specification provides an adequate written description of the claimed variants of SEQ ID NO:2 to convey with reasonable clarity to those skilled in the art that Applicants were in possession of the invention as "now" claimed at the time of filing of this application.

Moreover, the Office Action asserts that the claims are related to "polypeptides having diverse functions are encompassed by the phrase 90-99% identity" or "a polynucleotide that would be 90-99% identical to SEQ ID NO:2 and that would still maintain the function of the polypeptide." However, Applicants teach 90-99% variants of SEQ ID NO:1 and SEQ ID NO:2 based on both sequence identity and functional activity which can be assessed using the assay of Example X and the interpretation of such an assay as seen in the results of the activity assays of PDE9A as shown in Figures 3-5. The amendments to claims 3 and 11 which now recite the function of the claimed invention, i.e., having cyclic nucleotide phosphodiesterase activity, rendering the Office's assertion moot. Accordingly, the Specification provides an adequate written description of the claimed polynucleotide and polypeptide sequences to convey with reasonable clarity to those skilled in the art that Applicants were in possession of the invention as "now" claimed at the time of filing of this application. Therefore, Applicants respectfully request withdrawal of this rejection.

Objection t Claim 12 und r 37 C.F.R. § 1.75(c)

Although not acquiescing in the stated reason for the objection to claim 12, claim 12 has been canceled and therefore objection to claim 12 is rendered moot.

Double Patenting Rejection, Statutory Type

Although not acquiescing in the stated reason for the rejection of claims 4, 9 and 23, claims 4, 9 and 23 have been canceled, hence issues pertaining to claims 4, 9 and 23 are rendered moot.

Double Patenting Rejection, Non-statutory Type

Claims 3, 6-8 and 11 stand rejected under the judicially created doctrine of obviousness-type double patenting, as being unpatentable over claims 1 and 3-8 of U.S. Patent No. 5,922,595.

In the interest of expediting prosecution of the instant application, Applicants submit herewith a Terminal Disclaimer with respect to U.S. Patent No. 5,922,595. Withdrawal of this rejection is therefore requested.

Rejection of Claim 12 under 35 U.S.C. §102 (a)

Although not acquiescing in the stated reason for the rejection of claim 12, claim 12 has been canceled and therefore rejection of claim 12 is rendered moot.

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CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact Applicants' Agent at (650) 621-8555

Please charge Deposit Account No. **09-0108** in the amount of **$ 110.00** as set forth in the enclosed fee transmittal letter. If the USPTO determines that an additional fee is necessary, please charge any required fee to Deposit Account No. **09-0108.**

Respectfully submitted,

INCYTE GENOMICS, INC.

Date: 27, November 2002

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

The first paragraph of page 1 has been amended as follows:

This application is a divisional application of U.S. application Serial Number 09/240,359 filed January 29, 1999, issued on July 3, 2001, as U.S. Patent No. 6,255,456, entitled CYCLIC GMP PHOSPHODIESTERASE, which is a divisional application of U.S. application Serial Number 08/987,466 filed December 9, 1997, issued on July 13, 1999, as U.S. Patent No. 5,922,595, entitled CYCLIC GMP PHOSPHODIESTERASE, the contents of all which are hereby incorporated by reference.

IN THE CLAIMS:

Claims 4, 9, 12 and 23 have been canceled.

Claims 3, 8 and 11 have been amended as follows:

3. **(Twice Amended)** An isolated polynucleotide encoding a polypeptide selected from the group consisting of:

a.) a polypeptide comprising the amino acid sequence of SEQ ID NO:1,

b) a polypeptide comprising [a naturally-occurring] an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1, said polypeptide having cyclic nucleotide phosphodiesterase activity,

c) a fragment of a polypeptide having the amino acid sequence of SEQ ID NO:1, said fragment having cyclic nucleotide phosphodiesterase activity, and

d) an immunogentic fragment of a polypeptide having the amino acid sequence of SEQ ID NO:1.

8. **(Twice Amended)** A method for producing a polypeptide encoded by the polynucleotide of claim 3, the method comprising:

a) culturing a cell under conditions suitable for expression of the polypeptide, wherein said cell is transformed with a recombinant polynucleotide, and said recombinant [poynucleotide] polynucleotide comprises a promoter sequence operably linked to a polynucleotide of claim 3, and

b) recovering the polypeptide so expressed.

11. **(Twice Amended)** An isolated polynucleotide selected from the group consisting of:

a) a polynucleotide comprising the polynucleotide sequence of SEQ ID NO:2,

b) a polynucleotide comprising a [naturally-occurring] polynucleotide sequence at least 90% identical to the polynucleotide sequence of SEQ ID NO:2, encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:1 and said polypeptide having cyclic nucleotide phosphodiesterase activity,

c) a polynucleotide complementary to a polynucleotide of a),

d) a polynucleotide complementary to a polynucleotide of b) and

e) an RNA equivalent of a)-d).